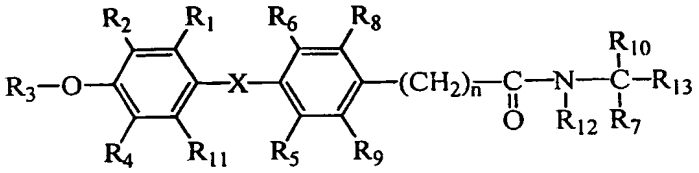
CLAIMS

1. A Compound of the general formula:



I

or a pharmaceutically acceptable salt thereof, wherein:

R_1 is selected from a group consisting of hydrogen, halogen, and C_1 to C_6 alkyl;

R_2 is selected from the group consisting of halogen, C_1 to C_6 alkyl, C_2 to C_6 alkenyl, C_2 to C_6 alkynyl, C_4 to C_7 cycloalkenyl, C_3 to C_7 cycloalkoxy, $SO_2(NR_{14}R_{15})$, $N(R_{16})SO_2R_{17}$, SR_{17}, SOR_{17}, SO_2R_{17}, COR_{16}, and $CR_{18}(OR_{16})R_{19}$; or R_2 is hydrogen when R_4 is alkyl and R_1 is halogen;

R_3 is selected from the group consisting of hydrogen, alkyl, benzyl, aroyl, and alkanoyl;

R_4 is halogen, cyano or alkyl;

R_5 and R_6 are independently selected from hydrogen, halogen; cyano, C_{1-4} alkyl, C_3 to C_6 cycloalkyl; where at least one of R_5 and R_6 is not hydrogen;

R_7 and R_{10} are independently selected from hydrogen, halogen, aryl and alkyl, and R_7 and R_{10} may be joined so as to comprise a chain of 2 to 6 methylene groups to form a ring of 3 to 7-membered in size;

R_8 and R_9 are each independently selected from the group consisting of hydrogen, halogen, alkoxy, hydroxy (OH), cyano, and alkyl;

provided that not more than one of R_2, R_4, R_8 and R_9 are hydrogen;

R_{11} is hydrogen, halogen or alkyl;

R_{12} is hydrogen or alkyl;

R_{13} is carboxylic acid (COOH) or esters thereof, phosphonic and phosphinic acid or esters thereof, sulfonic acid, tetrazole, hydroxamic acid, thiazolidinedione, acylsulfonamide, or other carboxylic acid surrogates known in the art;

R_{14} and R_{15} for each occurrence are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl, and R_{14} and R_{15} may be joined so as to comprise a chain of 3 to 6 methylene groups to form a ring of 4 to 7-membered in size;

R_{16} is selected from a group consisting of hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl;

R_{17} is selected from a group consisting of alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl;

R_{18} and R_{19} for each occurrence are each independently selected from the group consisting of hydrogen, alkyl, cycloalkyl, aryl, heteroaryl, arylalkyl and heteroarylalkyl;

n is an integer of 0, 1 or 2;

X is selected from: -O-, $-CH_2-$, $-CF_2-$, -Se-, -NH-, -S-, -SO-, $-SO_2-$ and -CO-;

and pharmaceutically acceptable salts, prodrug forms and stereoisomers thereof.

2. A compound according to claim 1, which has one or more asymmetric centers and can exist in the form of racemates, single and multiple enantiomers, as individual diastereomers, with all possible isomers, and mixtures thereof.

3. A compound according to claim 1 or 2 said compound being:
N-[3,5-Dichloro-4-(4-hydroxy-3-isopropyl-5-methylphenoxy)benzoyl] glycine (**E1**);
N-[3,5-Dichloro-4-(3-bromo-4-hydroxy-5-isopropylphenoxy)benzoyl] glycine (**E2**);
N-[3,5-Dichloro-4-(2-bromo-4-hydroxy-5-isopropylphenoxy)benzoyl] glycine (**E3**);
N-[3,5-Dichloro-4-(3-chloro-4-hydroxy-5-isopropylphenoxy)benzoyl] glycine (**E4**);
N-[3,5-Dichloro-4-(3-cyano-4-hydroxy-5-isopropylphenoxy)benzoyl] glycine (**E5**);
N-[3,5-Dichloro-4-(3-fluoro-4-hydroxy-5-isopropylphenoxy)benzoyl] glycine (**E6**).
N-[3,5-Dichloro-2-methyl-4-(3-methyl-4-hydroxy-5-isopropylphenoxy)benzoyl] glycine (**E7**).
L-N-[3,5-Dibromo-4-(3-fluoro-4-hydroxy-5-isopropylphenoxy)phenylacetyl] valine (**E10**)
D-N-[3,5-Dibromo-4-(3-chloro-4-hydroxy-5-isopropylphenoxy)phenylacetyl] phenylglycine (**E11**)
L-N-[3,5-Dibromo-4-(4-hydroxy-3-isopropyl-5-methylphenoxy)phenylacetyl] valine (**E12**)
L-N-[3,5-Dibromo-4-(4-hydroxy-3-isopropyl-5-methylphenoxy)phenyl-acetyl]phenylglycine (**E13**)
L-N-[3,5-Dibromo-4-(3,5-dimethyl-4-hydroxyphenoxy)phenylacetyl]-phenylglycine (**E14**)

4. N-[3,5-Dibromo-2-methyl-4-(3-methyl-4-hydroxy-5-isopropylphenoxy)benzoyl] glycine (**E8**).
N-[3,5-Dimethyl-2-methyl-4-(3-methyl-4-hydroxy-5-isopropylphenoxy)benzoyl] glycine (**E9**).

5. A compound according to any one of claims 1 to 3 for use in medical therapy.

6. A pharmaceutical composition comprising an effective amount of a compound according to claim 1 to 3 or a pharmaceutically effective salt thereof, together with a pharmaceutically acceptable carrier.

7. A process for making a pharmaceutical composition comprising combining a compound according to any one of claims 1 to 3 and a pharmaceutically acceptable carrier.

8. A pharmaceutical composition comprising a compound according to any one of claims 1 to 3 and at least one additional therapeutic agent selected from the group consisting of other compounds of formula I, anti-diabetic agents, anti-osteoporosis agents, anti-obesity agents, growth promoting agents, anti-inflammatory agents, anti-anxiety agents, anti-depressants, anti-hypertensive agents, cardiac glycosides, cholesterol/lipid lowering agents, appetite supressants, bone resorption inhibitors, thyroid mimetics, anabolic agents, anti-tumor agents and retinoids.

9. The pharmaceutical composition of claim 8 wherein said additional therapeutic agent is an antidiabetic agent selected from the group consisting of a biguanide, a glucosidase inhibitor, a meglitinide, a sulfonylurea, a thiazolidinedione, a PPAR-alpha agonist, a PPAR-gamma agonist, a PPAR alpha/gamma dual agonist, an SGLT2 inhibitor, a glycogen phosphorylase inhibitor, an aP2 inhibitor, a glucagon-like peptide-1 (GLP-1), a dipeptidyl peptidase IV inhibitor and insulin.

10. The pharmaceutical composition of claim 8 wherein said additional therapeutic agent is an antidiabetic agent selected from the group consisting of metformin, glyburide, glimepiride, glipyride, glipizide, chlorpropamide, gliclazide, acarbose, miglitol, troglitazone, pioglitazone, englitazone, darglitazone, rosiglitazone and insulin.

11. The pharmaceutical composition of claim 8 wherein said additional therapeutic agent is an anti-obesity agent is selected from the group consisting of an aP2

inhibitor, a PPAR gamma antagonist, a PPAR delta agonist, a beta 3 adrenergic agonist, a lipase inhibitor, a serotonin reuptake inhibitor, a cannabinoid-1 receptor antagonist and an anorectic agent.

12. The pharmaceutical composition of claim 8 wherein said additional therapeutic agent is a hypolipidemic agent selected from the group consisting of a thiazolidinedione, an MTP inhibitor, a squalene synthetase inhibitor, an HMG CoA reductase inhibitor, a fibric acid derivative, an ACAT inhibitor, a cholesterol absorption inhibitor, an ileal Na^+/bile cotransporter inhibitor, a bile acid sequestrant and a nicotinic acid or a derivative thereof.

13. A method for preventing, inhibiting or treating a disease which is dependent on the expression of a T_3 regulated gene or associated with metabolic dysfunction, which comprises administering to a patient in need of treatment a therapeutically effective amount of a compound as defined in claims 1 to 3.

14. A method for treating or delaying the progression or onset of obesity, hypercholesterolemia, atherosclerosis, depression, osteoporosis, hypothyroidism, subclinical hyperthyroidism, non-toxic goiter, thyroid cancer, reduced bone mass, density or growth, eating disorders, reduced cognitive function, thyroid cancer, glaucoma, cardiac arrhythmia, congestive heart failure or a skin disorder or disease, which comprises administering to mammalian patient in need of treatment a therapeutically effective amount of a compound as defined in claim 1.

15. The method as defined in claim 13, wherein the said disease is obesity, hypercholesterolemia, atherosclerosis, depression, osteoporosis, hypothyroidism, goiter, thyroid cancer, glaucoma, cardiac arrhythmia, congestive heart failure, or skin disorders.

16. The method according to claim 14, wherein the skin disorder or disease is dermal atrophy, post surgical bruising caused by laser resurfacing, keloids, stria, cellulite, roughened skin, actinic skin damage, lichen planus, ichtyosis, acne, psoriasis,

Dernier's disease, eczema, atopic dermatitis, chloracne, pityriasis and skin scarring.

17. The method according to claim 13 further comprising administering, concurrently or sequentially, a therapeutically effective amount of at least one additional therapeutic agent selected from the group consisting of other compounds of formula I, anti-diabetic agents, anti-osteoporosis agents, anti-obesity agents, growth promoting agents, anti-inflammatory agents, anti-anxiety agents, anti-depressants, anti-hypertensive agents, cardiac glycosides, cholesterol/lipid lowering agents, appetite supressants, bone resorption inhibitors, thyroid mimetics, anabolic agents, anti-tumor agents and retinoids.

18. A method of treating or delaying the progression or onset of a skin disorder or disease which comprises administering to a mammalian patient a therapeutically effective amount of a compound as defined in claim 1 in combination with a retinoid or a vitamin D analog.

19. A method for treating or delaying the progression or onset of obesity which comprises administering to mammalian patient in need of treatment a therapeutically effective amount of a compound as defined in Claim 1.

20. A method according to claim 19 further comprising administering, concurrently or sequentially, a therapeutically effective amount of at least one additional therapeutic agent selected from the group consisting of an anti-obesity agent and an appetite suppressant.

21. A method according to claim 20 wherein said anti-obesity agent is selected from the group consisting of aP2 inhibitors, PPAR gamma antagonists, PPAR delta agonists, beta 3 adrenergic agonists, lipase inhibitors, serotonin (and dopamine) reuptake inhibitors, cannabinoid-1 receptor antagonists, other thyroid receptor agents and anorectic agents.

22. The use of a compound according to any of claims 1 to 4 in the preparation of a medicament to inhibit or treat a disease which is dependent on the expression of a T_3 regulated gene or associated with metabolic dysfunction.

23. The use according to claim 22, wherein said disease is selected from obesity, hypercholesterolemia, atherosclerosis, depression, osteoporosis, hypothyroidism, subclinical hyperthyroidism, non-toxic goiter, thyroid cancer, reduced bone mass density or growth, eating disorders, reduced cognitive function, thyroid cancer, glaucoma, cardiac arrhythmia, congestive heart failure or a skin disorder or disease.

24. The use according to claim 23, wherein the skin disorder or disease is selected from dermal atrophy, post surgical bruising caused by laser resurfacing, keloids, stria, cellulite, roughened skin, actinic skin damage, lichen planus, ichtyosis, acne, psoriasis, Dernier's disease, eczema, atopic dermatitis, chloracne, pityriasis and skin scarring.

25. Use according to claim 22 in combination with at least one additional therapeutic agent selected from the group consisting of other compounds of formula I, anti-diabetic agents, anti-osteoporosis agents, anti-obesity agents, growth promoting agents, anti-inflammatory agents, anti-anxiety agents, anti-depressants, anti-hypertensive agents, cardiac glycosides, cholesterol/lipid lowering agents, appetite supressants, bone resorption inhibitors, thyroid mimetics, anabolic agents, anti-tumor agents and retinoids.

26. Use according to claim 22 in combination with a retinoid or a vitamin D analog wherein said disease is a skin disorder or disease.

27. Use according to claim 22 wherein said disease is obesity.

28. Use according to claim 27 in combination with at least one additional therapeutic agent selected from the group consisting of an anti-obesity agent and an appetite suppressant.

29. Use according to claim 28, wherein said anti-obesity agent is selected from the group consisting of aP2 inhibitors, PPAR gamma antagonists, PPAR delta agonists, beta 3 adrenergic agonists, lipase inhibitors, serotonin (and dopamine) reuptake inhibitors, cannabinoid-1 receptor antagonists, other thyroid receptor agents and anorectic agents.

30. A pharmaceutical composition which functions as a selective agonist of the thyroid hormone receptor comprising a compound as defined in claim 1.